Lu ran

The Fight Against Viral Diseases

RESEARCH AND INNOVATION AT LUTRAN

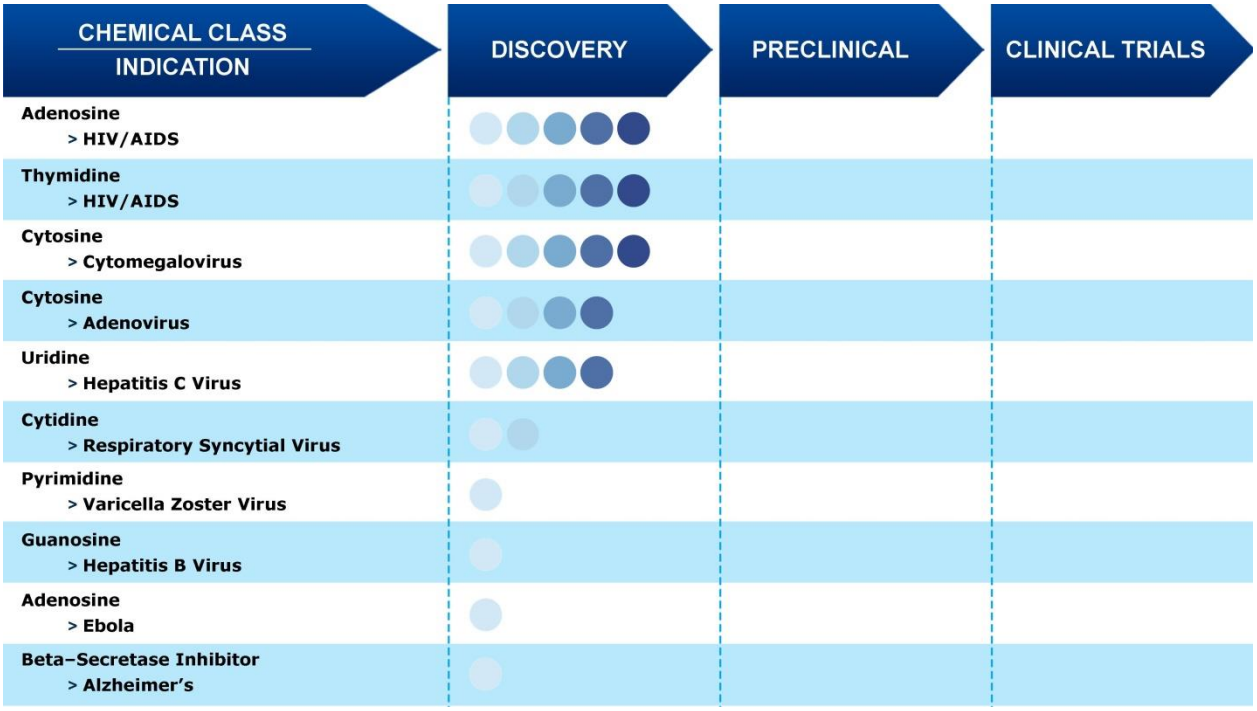
LuTran Inc. is a dynamic, innovation–driven pharmaceutical research company located in the heart of Silicon Valley, where we push the boundaries of medical science to discover and develop novel medicines for some of the world's most debilitating viral and neurological diseases: from AIDS through biosafety level 4 viruses, including Ebola hemorrhagic fever and Alzheimer's.

LEADERSHIP > Ronald Griffith, Ph.D. is the Director and Chief Science Officer for LuTran. Ron is a senior executive with over 30 years of research and development experience in both pharmaceutical and biotechnology companies. He is experienced with the complete drug development process from IND through NDA with world class hands–on expertise for drug discovery and development in virology and neurological diseases. He has published over 150 patents and publications with a career of 18 compounds to IND and 3 compounds to FDA registration.

MEDICINAL CHEMISTRY > Our chemistry can improve binding affinity and intrinsic potency through stronger hydrophobic synergies in the target receptor, increase duration of action by being resistant to CYP metabolism and consequently improve bioavailability and enhance safety through maximizing specific hydrophobic interactions.

OUR PHARMACEUTICAL PIPELINE FOR THE FIGHT AGAINST VIRAL AND ALZHEIMER'S

DEVELOPMENT > LuTran has a promising portfolio of 10 compounds in development against the viruses of HIV, HBV and HCV, ADV, Ebola, HCMV, RSV, VZV and Alzheimer's. Furthermore, we have in the discovery stage several best–in–class compounds where we may improve efficacy and enhance the safety profiles towards our drug targets, including hemorrhagic fevers.



OUR UNCONDITIONAL PLEDGE IN THE BETTERMENT OF VIRAL RESEARCH

> NOVEL EFDA ANALOG AND FESTINAVIR ANALOG FOR HIV/AIDS

Even though EFdA analog is less potent than EFdA, EFdA analog is still one of the most potent compounds discovered against HIV.

EFdA analog has >2X improved IV half–life, improved oral half–life and oral bioavailability in rats in comparison to EFdA.

Potentially EFdA analog may be similar to EFdA and because of our significantly lower research and development costs we could be more advantageous in cost with distribution to patients.

Festinavir analog has >2X improved IV half–life, 9X improved oral half–life and improved oral bioavailability in rats in comparison to festinavir (censavudine). We have a significantly improved oral half–life in rats indicating once a day dosing for festinavir analog in comparison to festinavir with 2–3 a day dosing.

DATA SUMMARY

HIV–1 MT2rep Assay	IC_{50} (µM)	CC_{50} (µM)
Reference: EFdA	0.00056	>150
Novel: EFdA analog	0.01308	>150
Reference: festinavir	1.3875	>150
Novel: festinavir analog	2.6355	>150

Pharmacokinetics in Male SD Rats	Oral F (%)	IV $T_{1/2}$ (h)
Reference: EFdA	58.6	0.568
Novel: EFdA analog	66.6	1.14
Reference: festinavir	173	0.49
Novel: festinavir analog	207	1.2

MARKET SUMMARY

The HIV drug regimens of Truvada, Stribild, Complera, Viread (Gilead Sciences, Inc.) and Atripla (Bristol–Meyers Squibb Company and Gilead Sciences, Inc.) all part of a drug combination including tenofovir disoproxil fumarate, had over a 50% market share of HIV therapeutics where global annual sales accounted for $24 billion (IMS Health Ltd, IMS MIDAS, 2015).

> NOVEL SOFOSBUVIR ANALOG FOR HEPATITIS C

We have improved potency in HCV GT1a replicon and permeability by about 10,000X in the PAMPA assay indicating improved bioavailability and efficacy for sofosbuvir analog in comparison to sofosbuvir.

DATA SUMMARY

HCV GT1a (H77) Replicon EC_{50} and CTX (Huh7) CC_{50} Assay	EC_{50} (µM)	CC_{50} (µM)
Reference: sofosbuvir	0.07209	>150
Novel: sofosbuvir analog	0.05426	102.4

Permeability Rate in PAMPA Assay	log PE	Ranking
Reference: sofosbuvir	−9.90	Low
Reference: propranolol	−4.96	High
Reference: furosemide	−10.09	Low
Novel: sofosbuvir analog	−5.62	Intermediate

MARKET SUMMARY

SOVALDI® SOFOSBUVIR 400 mg TABLETS

Harvoni (ledipasvir/sofosbuvir–Gilead Sciences, Inc.) was the top–selling prescription drug in the world with over $18 billion in global sales in 2015 (IMS Health, 2016) for HCV therapy. Sovaldi (sofosbuvir) ranked eighth, with $6.6 billion in sales.

> NOVEL CIDOFOVIR ANALOG FOR CYTOMEGALOVIRUS

Cidofovir analog is >6X more potent towards HCMV with a therapeutic index being >6 times safer than cidofovir. Cidofovir analog has similar oral bioavailability and half–life to cidofovir in rats.

DATA SUMMARY

HCMV AD169 GFP Assay	EC50 (µM)	CC50 (µM)	SI
Reference: cidofovir	9.78	>100	>10.22
Reference: ganciclovir	13.77	>100	>7.26
Novel: cidofovir analog	1.56	>100	>64.06

Pharmacokinetics in SD Rats	Oral F (%)	IV $T_{1/2}$ (h)
Reference: cidofovir	8	1.35
Novel: cidofovir analog	7.11	1.58

MARKET SUMMARY

CHIMERIX

Chimerix, Inc. is developing brincidofovir for HCMV and ADV with a market capitalization of $221 million (May 2017).

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